§ 1.121(b)(1)(i) and (ii). Applicants also attach Appendix A with marked up amendments indicated with brackets and underlining as required under 37 C.F.R. § 1.121(b)(1)(iii).

CONCLUSION

In light of the Amendments and Remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to contact the undersigned attorney or Cathryn Campbell with any questions related to this application.

Respectfully submitted,

June 27, 2003
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APPENDIX A

Please amend the paragraph on page 29 to read as follows:

A genetic variation can be readily obtained from a variety of public sources or can be routinely prepared using, for example, standard mutagenesis procedures. For example, a series of parent *Drosophila* strains, each containing one of a series of genetic variations, can be obtained from The Bloomington *Drosophila* Stock Center at Indiana University (Bloomington, IN), a public repository containing about 7000 fly stocks including a variety of deficiency stocks and stocks carrying mutant alleles of particular genes. A complete list of stocks is available on **[the Internet at http://www.flystocks.bio.indiana.edu.] the world wide web at flystocks.bio.indiana.edu**.

Please amend the paragraph bridging pages 35 and 36 to read as follows:

Control siblings can be conveniently identified in *Drosophila* using balancer chromosomes. As used herein, the term "balancer chromosome" means a multiply inverted *Drosophila* chromosome usually carrying a dominant marker mutation. One skilled in the art understands that a useful balancer chromosome carries multiple chromosomal inversions and suppresses recombination along the full length of the chromosome. A balancer chromosome also can carry a dominant marker mutation

resulting in a phenotype such as a particular eye color or wing phenotype that can be readily identified in flies carrying the balancer. In addition, a balancer chromosome may contain one or more recessive marker mutations for easy identification of progeny carrying two copies of the balancer during segregation analysis. Balancer chromosomes are available for the X, second, and third *Drosophila* chromosomes: for example, *FM7a*, *FM7b* and *FM7c* are convenient X chromosome balancers; *SM6* and *In(2LR)O, Cy* dp^{lv1} *pr* cn^{2} are convenient balancers for the second chromosome; and *TM3, TM6, TM6B* and *TM8* are convenient balancers for the third chromosome. Balancer chromosomes can be obtained from The Bloomington *Drosophila* Stock Center at Indiana University. A complete list of available balancer chromosomes is available **[at http://www.flystocks.bio.indiana.edu.] on the world wide web at flystocks.bio.indiana.edu**. Methods of constructing stocks utilizing balancer chromosomes are well known in the art as described, for example, in Greenspan, *supra*, 1997.

Please amend the paragraph bridging pages 64 and 65 to read as follows:

Sequence analysis using the BLAST program **[at either the Berkeley *Drosophila* Genome Project <http://www.fruitfly.org/blast/> or NCBI <http://www.hcbi.nlm.nih.gov/BLAST/>] on the world wide web at either the Berkeley *Drosophila* Genome Project website or at the NCBI website** revealed that about 15% of the transcripts

represented sequences currently available in *Drosophila* databases (Table 4). In particular, the following genes were identified with altered RNA expression levels in *Appl*^{d} flies. *Shibire* (*shi*), which encodes dynamin (van der Bliek and Meyerowitz, Nature 351:411-414 (1991)); *cap-n-collar* (*cnc*), which encodes a bZIP-like transcription factor (Mohler et al., Mech. Dev. 34:3-9 (1991)), *Pbprp-2*, which encodes a pheromone-binding-protein-related-protein (Pikielny et al., Neuron 12:35-49 (1994)); *RpL9*, encoding ribosomal protein L9 (Schmidt et al., Mol. Gen. Genet. 251:381-387 (1996)); *Dhod* (Jones et al., Mol. Gen. Genet. 219:397-403 (1989)), 18S ribosomal RNA; *Tat-binding protein-1 (Tbp-1*, FlyBase FBgn0026321) of the proteasome; and a homolog of rat *exo84* of the exocyst secretion complex (Kee et al., Proc. Natl. Acad. Sci. USA 94:14438-14443 (1997)).

Please amend the paragraph at page 65, lines 7-20 to read as follows:

mRNA levels also were compared using a DNA microarray made from 400 randomly chosen ESTs from the Berkeley *Drosophila* Genome Project UniGene **[Library (http://ww.fruitfly.org/EST/).] Library, which can be found on the world wide web**. Briefly, a glass slide DNA microarray was prepared as described in White et al., Science 286:2179-2184 (1999), from the UniGene Library (plates #54, 55, 56 and 57; Research Genetics, Huntsville, AL). PolyA+ RNA was prepared from groups of 100 whole flies using

MicroPoly(A)Pure (Ambion, Austin, TX) according to the manufacturer's instructions, and subsequently labeled and hybridized to the arrays as described in White et al., *supra*, 1999. ESTs showing >2-fold expression difference were analyzed as described above.